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添付公開書類:
— 国際調査報告書

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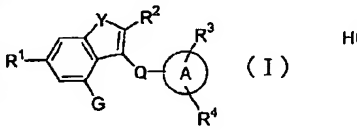
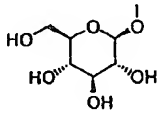
(54) Title: FUSED HETEROCYCLIC DERIVATIVE, MEDICINAL COMPOSITION CONTAINING THE SAME, AND MEDICINAL USE THEREOF

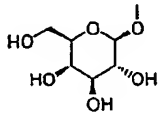
(54) 発明の名称: 縮合複素環誘導体、それを含有する医薬組成物およびその医薬用途



(I)



(G1)



(G2)

(57) Abstract: A fused heterocyclic derivative represented by the general formula (I) (wherein R^1 is hydrogen, OH, etc.; R^2 is hydrogen, halogeno, or alkyl; R^3 and R^4 each is hydrogen, OH, halogeno, etc.; Q is alkylene, etc.; ring A is aryl or heteroaryl; and G is the group represented by the formula (G1) or (G2)), (G1) (G2) a pharmacologically acceptable salt of the derivative, or a prodrug of either. They have excellent inhibitory activity against human SGLT and are useful as preventive or therapeutic agents for diseases attributable to hyperglycemia, such as diabetes, postprandial hyperglycemia, impaired glucose tolerance, complications of diabetes, and obesity.

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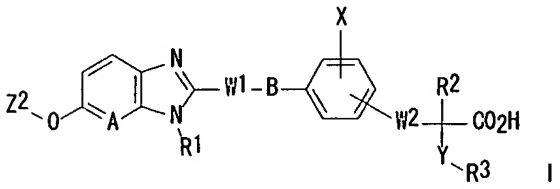
WO 2004/087727 A1

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:516372 CAPLUS <<LOGINID::20060731>>
DN 137:78955
TI Preparation of benzimidazole-α-substituted carboxylic acid derivatives for prevention and/or treatment of diseases such as diabetes
IN Fujita, Takashi; Wada, Kunio; Oguchi, Minoru; Honma, Hidehito; Fujiwara, Toshihiko; Iwabuchi, Haruo
PA Sankyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 93 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2002193948	A2	20020710	JP 2001-308762	20011004 <—
PRAI	JP 2000-307158	A	20001006		

OS MARPAT 137:78955
GI



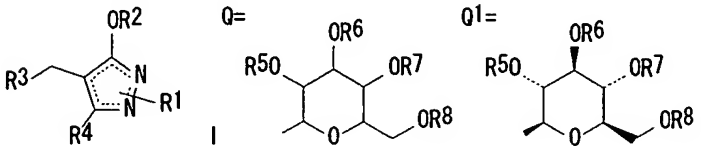
I

AB Disclosed are insulin-resistance improving agents, blood sugar-lowering agents, immune regulating agents, aldose reductase-inhibitors, 5-lipoxygenase-inhibitors, lipid peroxide formation-suppressing agents, peroxisome proliferator-activated receptor (PPAR)-activating agents leukotriene antagonists, fat cell-formation promoters, and calcium antagonists containing the title compds. [I; R1, R2, R3 = H, C1-6 alkyl, (un)substituted C6-10 aryl, (un)substituted C7-16 , C1-6 alkylsulfonyl, C1-6 haloalkylsulfonyl, (un)substituted C6-10 arylsulfonyl, C7-16 aralkylsulfonyl; A = N, CH; B = O, S; W1 = C1-6 alkylene; W2 = single bond, C1-8 alkylene; X = H, C1-6 alkyl, C1-6 haloalkyl, C1-6 alkoxy, halo, HO, cyano, NO2, C3-10 cycloalkyl, (un)substituted C6-10 aryl, (un)substituted C7-16 aralkyl, C1-7 aliphatic acyl, C4-11 cycloalkylcarbonyl, (un)substituted C7-11 arylcarbonyl, C8-17 aralkylcarbonyl, (un)substituted monocyclic heterocyclylcarbonyl, CONH2, (un)substituted C7-11 arylaminocarbonyl, (un)substituted NH2; Y = O, S(O)p (p = 0-2); Z2 = (un)substituted saturated heterocyclyl or C6-10 aryl] or pharmacol. acceptable salts as the active ingredients. They are useful for the prevention and/or treatment of diabetes, impaired glucose tolerance, neurosis, cataract, coronary artery disease, and gestational diabetes. Thus, a solution of 3-[4-[[[[4-[4-(adamantan-1-yl)phenoxy]-2-(N-tert-butoxycarbonyl-N-methylamino)phenyl]amino]carbonyl]methoxy]phenyl]-2-(4-fluorobenzyloxy)propionic acid Me ester in 4 N HCl/dioxane was stirred at room temperature for 1 h to give 3-[4-[6-[4-(adamantan-1-yl)phenoxy]-1-methyl-1H-benzimidazol-2-ylmethoxy]phenyl]-2-(4-fluorobenzyloxy)propanoic acid Me ester which was stirred with a mixture of 2 n aqueous NaOH and methanol at room temperature for 2 h, treated with THF, stirred for 4 h, poured into water, and neutralized with HCl and aqueous NaHCO3 to give 3-[4-[[6-[4-(adamantan-1-yl)phenoxy]-1-methyl-1H-benzimidazol-2-yl]methoxy]phenyl]-2-(4-fluorobenzyloxy)propanoic acid (II). When a feed containing 0.01% II was fed to diabetic KK mice for 3 days, blood sugar level was lowered by 58.5%. A capsule, a tablet, and a granule formulation containing II were prepared

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:36456 CAPLUS <<LOGINID::20060731>>
DN 138:90016
TI Preparation of 3-pyrazolyl glycosides for treatment of diabetes
IN Shirakura, Shiro; Ito, Yasuhiko; Kusaka, Hiroko; Kusaka, Hideaki; Takeshita, Kenichi; Matsumoto, Yoshiko; Abe, Masayuki; Ota, Yoshihisa; Nomoto, Yuji
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2003012686	A2	20030115	JP 2001-200388	20010702 <—
PRAI	JP 2001-200388		20010702		

OS MARPAT 138:90016
GI



AB 3-Pyrazolyl glycosides, in particular 3-pyrazolyl β-D-glucopyranosides [I; R1 = H, (un)substituted lower alkyl or lower alkoxy; R4 = (un)substituted lower alkyl or lower alkoxy; R5-R8 = H, hydroxy-protecting group; when at least one of R5-R8 is a hydroxy-protecting group and R5-R8 is H and also R1 is (un)substituted lower alkyl or lower alkoxy, R3 is (un)substituted aryl or heterocyclyl; or when R5-R8 is H and R1 is H or lower alkyl, R3 is p-(un)saturated lower alkylsulfonylaryl, or substituted aryl, or (un)substituted aromatic heterocyclyl] or pharmacol. acceptable salts thereof are prepared Also disclosed are preventives or remedies for diabetes or diabetes complications, blood sugar-lowering agents, or Na+-glucose cotransporter (sodium-glucose cotransporter) (SGLT) inhibitors containing the above compds. I as the active ingredients. Thus, to a solution of 4.00 g 1,2-dihydro-4-[(4-methylthiophenyl)methyl]-5-trifluoromethyl-3H-pyrazol-3-one and 14.78 g 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl bromide in 300 mL MeCN was added 9.69 g K2CO3 and stirred at room temperature for 3 days to give 58% 4-[(4-methylthiophenyl)methyl]-3-[(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)oxy]-5-trifluoromethyl-1H-pyrazole which (908 mg) was stirred with a mixture of 15 mL ethanol and 5ml aqueous K2CO3 at room temperature for 1 h to give 7% 4-[(4-methylthiophenyl)methyl]-3-[(β-D-glucopyranosyl)oxy]-5-trifluoromethyl-1H-pyrazole (II). To a solution of 22 mg II in 1 mL MeOH was added 7 mg m-chloroperbenzoic acid and stirred at room temperature for 4 h to give 20% 4-[(4-methylsulfinylphenyl)methyl]-3-[(β-D-glucopyranosyl)oxy]-5-trifluoromethyl-1H-pyrazole (III). In a SGLT inhibition assay, III showed IC50 of 0.0466 μM for inhibiting the uptake of [14C]AMG in proximal tubule epithelial cell lines (LLC-PK1). III at 1 mg/kg i.v. increased the urinary excretion of glucose from 502±61 μg/2 h (control) to 62,077±10,456 μg/2 h in male SLC SD rats.